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FINE STRUCTURE OF THE TRANSITIONAL EPITHELIUM OF THE DOG URETER

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The fine structure of the transitional epithelium of adult dog ureter has been studied in thin sections with an electron microscope.

It is thought that the light cells represent an active stage and that the dark cells represent a less active stage of the same cell type according to the shape of nucleus and cell organella. The dark cells are also considered as a type to be the result of pressure by adjacent cells or newly formed cells.

The free luminal surface of the cells and many cytoplasmic vesicles in these cells are bounded by a thick unit membrane. These vesicles or vacuoles are considered to function as a defense of the cytoplasm, when the epithelial cells change the form. The vesicles and the plasma membrane maintain angular conformations which suggest the membrane to be unsually rigid. It is supposed that the plasma membrane of the superficial cells is the major barrier to the free flow of water from the cytoplasma into the hypertonic urine. The possible origin of the thick plasma membrane in the Golgi apparatus was shown.

All the cells of the epithelium have a dense feltwork of tonofilaments which ramify throughout the cytoplasm. The tonofilaments connect frequently with intercellular desmosomes. Keratohyalin-like granules were seen in the tonofilaments.

INTRODUCTION

The ureter is a slightly flattened tube that extends from the end of the renal pelvis to the bladder. The ureteral epithelium is composed of the transitional one, however its function is not known. The present investigation is concerned with two aspects of a permeability barrier to the urine and a defence to the damage of the cytoplasm of the transitional epithelial cells. The transitional epithelium lining the ureters is in contact with strongly hypertonic urine. This epithelium must, therefore, have a permeability barrier to prevent a continual inflow of water and dilution of the urine from the cellular fluid of the urothelium.

It is thought that a further electron microscopic investigation of the ureteral epithelium, with special reference to a possible permeability barrier, would provide with the morphological bases for physiological studies.

MATERIALS AND METHODS

The materials used for the present study consist of 9 randomly autopsied dogs.

The ureters were removed from all cases and fixed in 10% formalin saline for the light microscopy. Paraffin sections were routinely stained with hematoxylin-eosin. For the electron microscopy, small pieces of the ureter were prepared and immediately fixed in 2% phosphate-buffered glutaraldehyde (pH 7.4) and then fixed in 2% osmium tetroxide (pH. 7.4). After dehydration through a graded ethanol series, the specimens were embedded in Epon 812. These thin sections were stained with uranyl acetate and lead citrate, and observed with a Hitachi HU-12A electron microscope.

RESULTS

The ureteral epithelium of the normal adult dog has a well-developed pattern of cell differentiation, with large, squamous,

complex cells in shape at the luminal surface and smaller, more simlified cuboidal or columnar cells forming the intermediate and basal layers (Fig. 1). The cells of the basal layer are attached by half desmosomes on their basal membranes to a basement membrane. The basal and intermediate cells and the lateral and basal membranes of the sqamous cells are deeply interdigitated (Fig. 2).

The epithelial cells of a ureter of the adult dog have been divided into light cells and dark cells, primarily on difference in density of the cytoplasm. The light cells are more numerous than the dark ones and the light cells are larger than the dark cells; the former usually has larger and round nuclei and the latter has smaller and irregular ones (Fig. 3). The light cells contain a smaller Golgi apparatus, lysosomes, considerable glycogen granules, many free ribosomes, numerous cytoplas-

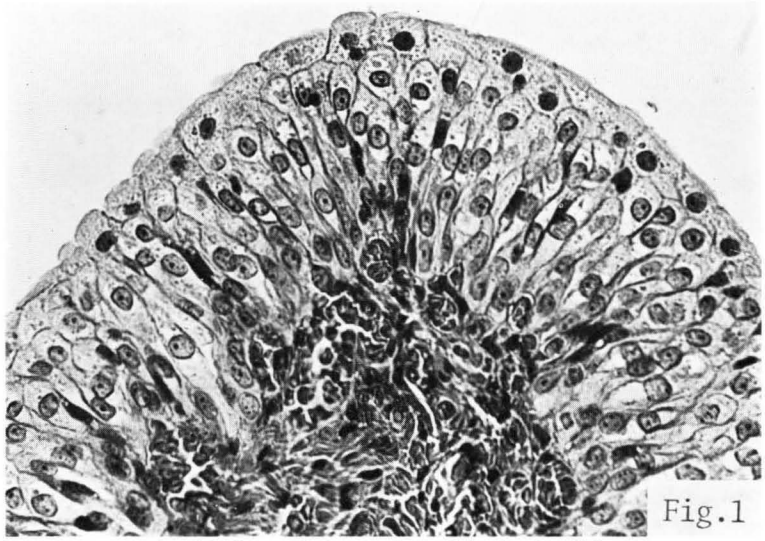

Fig. 1. The ureteral epithelium of the normal adult dog by light microscopy. ×400

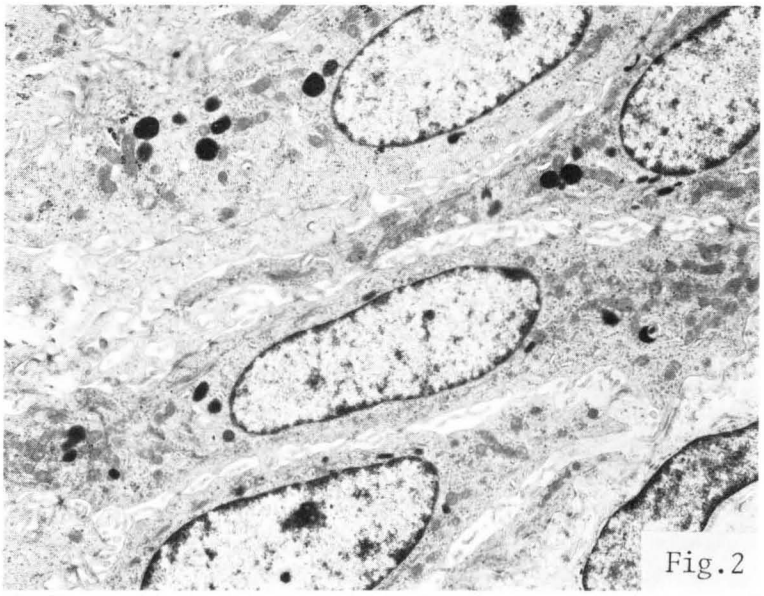

Fig. 2. The basal layer of the ureteral epithelium by electron microscopy. ×5,000

mic filaments, a few mitochondria and very small endoplasmic reticulum.

The surface sqamous cells at the luminal surface have several specialized features. The cells of the transitional epithelium have thick cell membrane (Fig. 4). The membrane toward the lumina of these cells is a three-layered structure, the width being greater than other cell plasma membranes. In some cases, it has a asymmetrical appearance, with the outer cell membrane being wider than the inner one (Fig. 4). The luminal membrane, when viewed by transmission electron microscopy, sometimes appeared to be raised with a pointed end as angular folds of the ure-

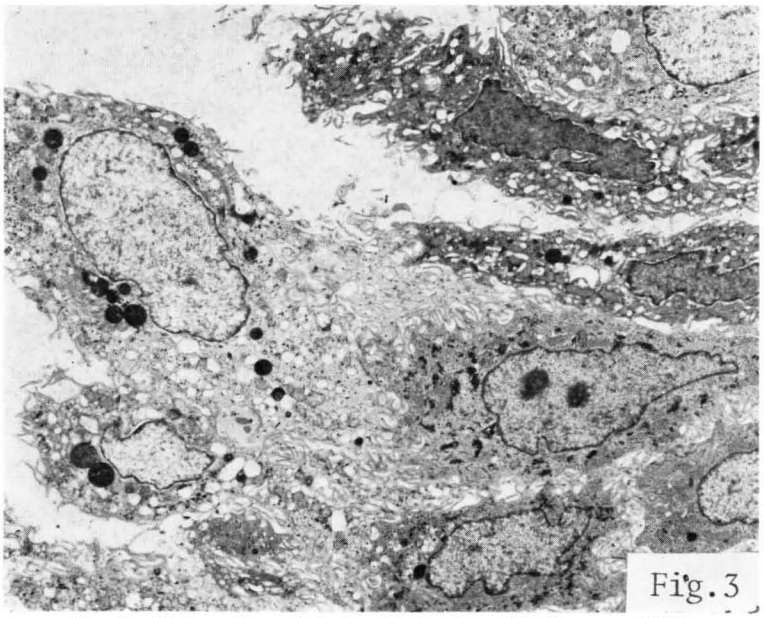

Fig. 3. Light cells and dark cells in the epithelium. ×1,500

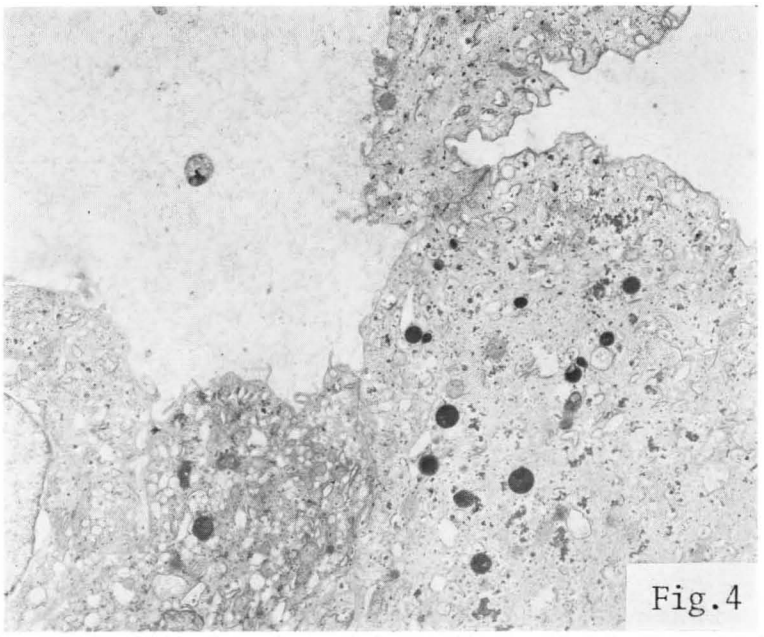

Fig. 4. The thick cell membrane of the transitional epithelial cells. ×4,000

teral lumen (Fig. 4, 5).

Vesicles or vacuoles in the same type of cell membrane width may be seen in the vicinity of the Golgi apparatus within the cytoplasm of the surface squamous cells (Fig. 5). The number, size and situation of vesicles or vacuoles are variable, some being large and approach to the luminal membrane, while others are small and iso lated from there. They may be flattened or roughly spherical in shape; the large ones often contain inclusions, and the inclusion frequently seems to be a core. The specialized vesicles or vacuoles seen near

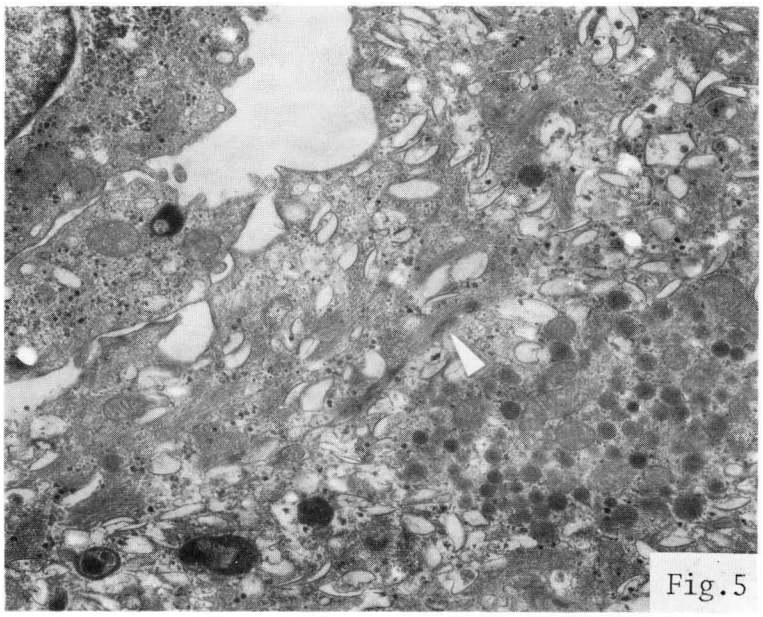

Fig. 5. The luminal cell membrane with pointed ends as angular folds of the ureteral lumen. ×10,000

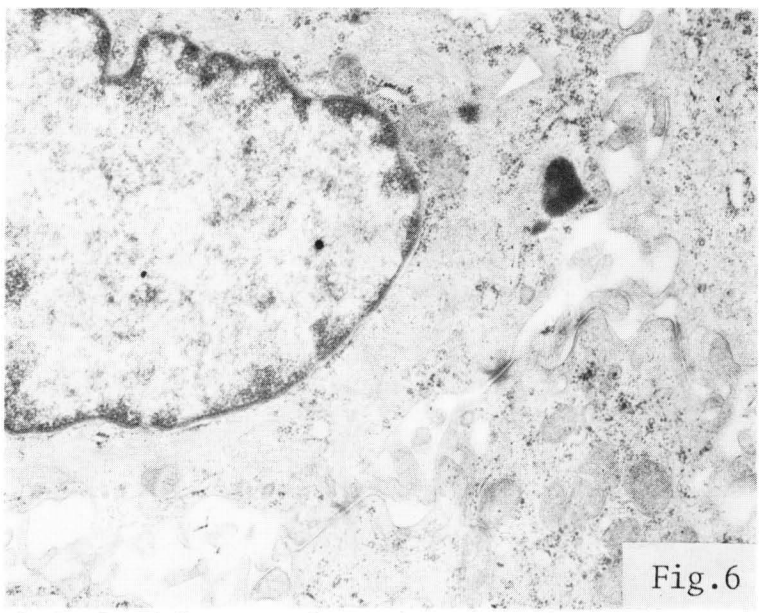

Fig. 6. Bundles of filaments terminate at desmosomes. Keratohyalin-like granules in the filaments. ×15,000

the lumen were not observed in the basal cells (Fig. 5).

Contiguous surface cells are united at the lumen by a continuous tight junction, which extends about 3 μm below the luminal surface. While these tight junctions are seen in all sections, passing through the contact between adjacent surface cells, desmosomes are frequently seen in ureteral epithelium of adult dog, suggesting that they are arranged intermittently around the cells (Fig. 4).

Numerous filaments are observed in the cells of ureteral epithelium. Bundles of filaments in the surface cells are larger and more numerous than in the basal cells, extending in many directions, and some of them terminate at desmosomes (Fig. 6).

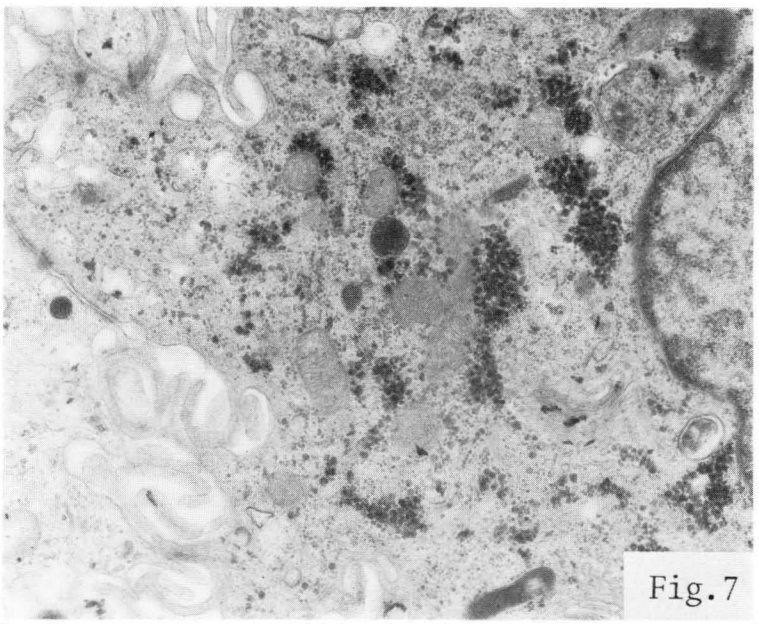

Fig. 7. Glycogen granules in the vicinity of the lysosomes or the filaments. ×15,000

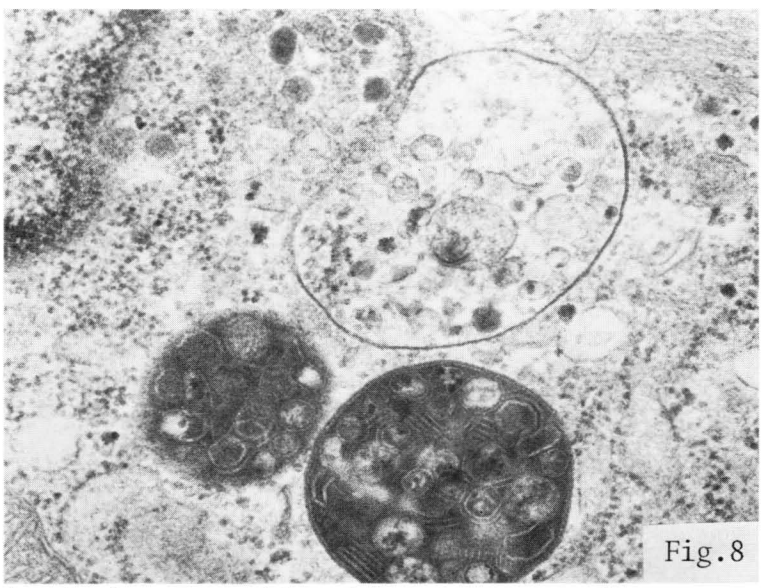

Fig. 8. Secondary lysosomes containing varied membranous or granular structures. ×35,000

Keratohyalin-like granules are observed in the filaments. The granules are electron dense spherical bodies and have no limiting membrane (Fig. 5 and 6△).

Large clusters of mitochondria are present within the surface squamous cells, as well as in the deeper layer. Rough-surfaced endoplasmic reticulums are sparse in all layers though ribosomes are plentiful.

The Golgi apparatus was moderately well developed, and often associated with primary lysosomes in the surface squamous cells. The Golgi apparatus was smaller in the intermediate and basal cells. The surface cells contained patches of glycogen granules and groups of mitochondria. Glycogen granules was seen in the vicinity of the lysosomes or the filaments (Fig. 7).

Secondary lysosomes were a striking feature of the epithelium of the ureter, being most frequent in the surface and intermediate layers; in the latter, they were often clustered around the nucleus. Ultrastructurally, lysosomes within the cytoplasm of epithelial cell of the ureter have an outer limiting membrane averaging 60 Å in diameter, and a finely granular matrix which contains a multitude of varied membranous and granular structures in secondary lysosomes (Fig. 8).

The intermediate and basal cells often showed large invagination of the nuclear membrane, and also the cells were of a simpler organization. The junction of the basal cells with the submucosa was irregular in shape, giving the appearance of microprotrusions of cytoplasm dipping into the submucosa. Intercellular junctions were folded in a complex manner and, occasionally, desmosomes were seen between intermediate cells.

DISCUSSION

The epithelial cells of the ureter are divided into light cells and dark ones based on difference in density of the cytoplasm. Hayakawa observed the dark cells in the urothelial tumor of the upper urinary tract[2]. It is considered that the light cells of the ureteral epithelium represent an active stage and that the dark cells represent a less active stage of the same cell type in the surface squamous or intermediate layers according to the shape of the nucleus and cell organella. The dark cells in the basal layer, however, are thought to have newly developed to have resulted. On the other hand, the dark cells are also considered as a type from pressure by ad jacent cells.

The superficial cells of the transitional epithelium have thick cell membranes. Patches of similar thick membrane are found in the walls of the Golgi cisternae[3,4]. The cell membrane of the inner luminal surface is thicker than the other parts of the cell. This is similar to the membrane structure observed in the epithelium of the urinary bladder of the mouse, rat and human[5,7]. The significance of thick cell membrane is to provide the defense to the free flow of water from the cytoplasm into the hypertonic urine. Examination of the surface by scanning electron microscopy shows that these surface features are actually small ridges and sulci[6,8~11]. The membrane may be flat or raised into angular folds of the ureteral lumen[12].

In the Golgi area of the superficial cells numerous vesicles or vacuoles with a membrane similar to the plasma membrane can be observed[1]. A small sac or bladder containing fluid or substance is vesicle, and a clear sac or bladder in low density is vacuole. The substance in the vesicles seems frequently to be a core. The Golgi areas in the superficial cells may produce vesicles or vacuoles. These facts suggest that the vesicles or vacuoles are the form in which the thicker membrane is manufactured and transported. Also, these vesicles or vacuoles are considered to be a defense mechanism of the cytoplasm, when the epithelial cells change the form.

The intracellular filaments can be divided according to their function. The cystoskeletal filaments are most abundant in the cells of ureteral epithelium, where they are referred to as tonofilaments. These tonofilaments extend in many directions in the cells and some of them ter-

minate at desmosomes. The tonofilaments provide these cells with rigidity, as well as variable size and shape. On the other hand, as the keratohyalin-like granules appear in the tonofilaments, it is considered that the tonofilaments would originate in the granules (Fig. 5, 6△).

Lysosomes are minute granular, membrane-bound organelles which contain enzymes for intracellular digestion. The lysosomes represent an essential part of the cellular defense and transport systems[4]. Structurally and functionally, lysosomes are divided into two categories: 1) primary lysosomes and 2) secondary lysosomes[1]. Secondary lysosomes are involved in enzymatic digestive activities, and therefore contain a collection of membranous and granular structures missing in the primary lysosomes. Koss[7] stated that the lysosomes in the cytoplasm of the ureteral epithelium store the useless or damaged asymmetric unit membrane. The vicinity of the centers of production of the lysosomes suggests the possibility of an association that is perhaps not casual but that serves the purpose of regulating the amount of production of asymmetric unit membrane by the Golgi apparatus.

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和文抄録

イヌ尿管移行上皮の微細構造

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武藤　浩・太田久美子・吉岡　郁夫

イヌ尿管の移行上皮を電顕で観察し，つぎのような結果を得た．上皮細胞は核の形や細胞内の小器官の状態により，機能の盛んな明細胞とそうでない暗細胞に分けられる．暗細胞はまた周囲から圧迫されたり，新生した細胞と考えられる．尿管の内腔面の細胞膜は厚く，上皮細胞内の小胞の膜も厚く，いずれも単位膜でできている．内腔面の細胞膜は尿と上皮細胞との間の隔壁となり，浸透圧から細胞を守るものであろう．上皮細胞内には tonofilament がよく発達し，一部は desmosome に連接する．tonofilament の発生は keratohyalin 様顆粒と関係があるらしい．